Magnetic Resonance Imaging with Intermolecular Double Quantum Coherences

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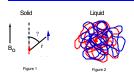
Introduction

In the 1960s, signals from "impossible" couplings in Nuclear Magnetic Resonance sparked the reevaluation of theoretical outlines for NMR. Up until the last decade, intermolecular dipolar couplings were argued to be averaged out by spatially random diffusion effects in liquid. Although this holds true for proximate spin pairs, dipolar interactions between protons separated by large distances as compared to average diffusion speed in solution were determined to be the source of these observed "impossible" signals. This effect was termed Intermolecular Zero/Double Quantum Coherences (ZQC/iDQC) by Dr. Warren S. Warren of Princeton University. In contrast, traditional MRI/fMRI signal stem from Single Quantum Coherences (SQC).

After the theoretical basis for quantification of dipolar interactions were developed, it was logical to expect and develop methods for observing iZQC/iDQC effects in Magnetic Resonance Imaging. Quantum filter gradients were added to simple gradient echo and spin echo sequences to create CRAZED (COSY revamped with asymmetric z-gradient echo detection) sequences.

This method poses novel contrasting capabilities as well as the ability to "tune in" to physiological features on par, in size, to what is known as the correlation distance, which can be controlled by gradient strength and duration. On the other hand, signal intensities from iZQC/iDQC measurements are significantly smaller than that from iSQC measurements.

Here we first present the origin of iZQC/iDQC from dipolar couplings in solution. A brief quantum mechanical outline of the theory behind iZQC/iDQC is then introduced. Optimum scanning parameters were simulated using Matlab 5.3. Finally, images obtained on phantom with SE and iDQC sequences are presented.

Intermolecular Dipolar Couplings Contribute to Signal

Solid   Liquid

Figure 1   Figure 2

Intermolecular dipolar couplings is a well-known phenomenon. However, such couplings were traditionally thought to be averaged out by molecular diffusion. In reality, spins separated by distances r_{ij} much greater than distance diffused within measurement time have a relatively constant r vector (as shown in figure 1). Thus dipolar couplings are NOT averaged out temporally.

$r_{ij} << x^2)^{1/2}$
$3\cos^2 - 1??0$
$D_{ij} ? [3\cos^2 _{ij} - 1]/r_{ij}^3$; 10 ms diffusion, $?x^2)^{1/2} = 7 \mu m$

$r_{ij} >> ? x^2)^{1/2}$
$3\cos^2 - 1$ unaffected

Figure 3

Figure 4

Using the iDQC CRAZED sequence, "impossible" NMR signals were obtained. Figure 4 shows evolution of magnetization vector under conventional MR theory following two RF and two gradient pulses. Projection onto x-y plane should give no signal!

Dipolar interaction from individual pairs of spins are miniscule and proportional to $1/r^3$, BUT the number of spin pairs increases with r^2. **Tiny dipolar couplings, when summed over vast number of spins, is proportional to 1/r !**

What are Intermolecular Zero/Double Coherences in Quantum Mechanical Terms?

Quantification of dipolar interactions proceeded in two directions. The "mean field treatment" involved modifying the Block equations, taking into account magnetic field corrections at each individual point due to dipolar couplings. The "coupled spin" treatment is quantum mechanical, involving the insertion of a dipolar Hamilton into the total Hamiltonian which evolves the entire system (density matrix).
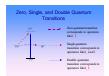
Both treatments were shown to give the same results [ref.2,3]. However, the "mean field treatment" is highly nonlinear, as can be expected from the large number of spins involved. The "coupled spin" treatment, owing to the elegance of quantum mechanics, offers a linear and highly intuitive picture. We will focus on the "coupled spin" treatment. Note: the high temperature approximation, which truncates all terms except SQC (or that normally observed in MRI) has to be discarded in this method.

In quantum mechanics, mathematical operators are defined by operators. Each quantum mechanical operator corresponds to a classical observable. For example, the Hamiltonian corresponds to total observed energy, while the "spin ½" operators correspond to spin angular momentum, which is crucial in the determination of magnetic dipole moment, and thus MRI signal intensity. In a one-spin system, the three spin ½ operators can be represented in matrix form as --

$I_z ? \begin{pmatrix} 1/2 & 0 \\ 0 & -1/2 \end{pmatrix}$ $I_x ? \begin{pmatrix} 0 & 1/2 \\ 1/2 & 0 \end{pmatrix}$ $I_y ? \begin{pmatrix} 0 & -i/2 \\ i/2 & 0 \end{pmatrix}$

In the spin ½ system, a spin can either be in the $?$ or $?$ state. For a $?$ spin to become a spin in the $?$ state, one quantum of energy must be absorbed. Two "ladder operators" are used to transform spins between its two spin states. These are –

$I_+ = I_x + iI_y$ $I_+ ???????$
$I_- = I_x - iI_y$ $I_- ????????$

Zero, Single, and Double Quantum Transitions

Zero, Single, and Double Quantum Coherence Operators

Every spin in the system is designated by a "spin ½" operator. Interacting pairs of spin can then be represented as $I_{x1}I_{x2}$, $I_{x1}I_{y2}$, etc.

Creation and Detection of iZQC/iDQC

In quantum mechanics, the entire system can be compactly represented by the density matrix, $?$. It contains all information concerning the system. **RF pulses and gradients can viewed as operators that "act" on the density matrix** At the end of each pulse sequence, the system has arrived at its final state, while still in the form of $?$. Depending on what kind of information we are seeking for, different basis sets and mathematical operations can be applied to $?$ to yield classical observables. In MRI, we want the magnetization in the x or y directions, which is calculated by

$M_x = <F_x ? = Tr (?F_x)$

where $F_x ? ?_i I_{xi}$

In iZQC/iDQC pulse sequences, the complete Hamiltonian which evolves the system has many components. In addition to the usual Zeeman field, chemical-shift, and J-coupling components, the **Dipolar Hamiltonian** has been inserted.

$H = H_{Zeeman} + H_{RF} + H_{J-Coupling} + H_{Chemical-Shift} + H_{dipolar}$

The basic scheme of iZQC/iDQC sequences is as follows :

RF gradients — Free evolution — Signal Detection

$?(0)$ — $?(int.)$ — $?(t)$

Creation of iZQC, iDQC, etc.

H_dipolar turns iZQC/iDQC into detectable SQC

Tr (?Fx) is detected

iDQC CRAZED Sequence and Parameter Optimization

Signal intensity can be written as

Two-quantum CRAZED sequence

$M_{DQ}^? (t_1, t_2) ? iM_0 e^{?/2? t_1} e^{/t_2} \sin? ^? \cos? ? 1??$
$?_{/t_2?_s}^{?_d} ?_2 ?_{/t_2?}^{?_{t_2}?} ? e^{?/t_{2,DQ}} e^{/t_2}$ [1] ref.1

Zero-quantum CRAZED sequence

$M_{ZQ}^? (t_1, t_2) ? i \frac{M_0}{E} e^{/t_2} J_1 \frac{?_{t_2}?}{?_d} e^{?/t_{2,ZQ}} e^{/t_2}$ [2] ref.4

where t_1 and t_2 are the evolution and detection time, respectively; M_0 is the equilibrium magnetization; $?$ is the resonance offset; J_2 is the second order Bessel function; $?_s =$

$T_{2,DQ}$ and $T_{2,ZQ}$ are T_2 relaxation rates in iDQC and iZQC sequences respectively, which might be different from T_2; dipolar demagnetizing time $?_d = (??_?? ?_?)^{-1}$ where $?$ is the gyromagnetic ratio and $?_?$ is the magnetic permeability constant.
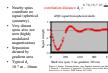
Figure 5

As shown here, when the second RF pulse is 60 or 300 degrees, iDQC signal is highest at both 1.5 and 3T.

iZQC/iDQC signal requires time to "grow" to its maximum value, in comparison to single quantum signals which appear immediately. Here signal is shown across t_2 (detection time).

Correlation Distance

correlation distance $d_c ? 7.5/7.8/? .57$

When spins are separated by half a helix pitch, or the correlation distance, iDQC signal is most significant. Notice that correlation distance can be controlled with gradient strength and duration.

iDQC Phantom Images on 3T

As mentioned above, dipolar coupling is a function of the angle $?$ in relation to the z magnetization with which the gradients are applied.

$D_{ij} ? 3\cos^2 ????$

At the so called "magic angle", $??54.7 ??$dipolar coupling between all spins (D_{ij}) go to zero. One would expect very low, if any, signal at the magic angle with the iDQC pulse sequence. Here we present images collected on silicon oil phantom at 3T machine using Spin Echo EPI and iDQC CRAZED EPI sequences at $??0??45 ??$and 54.7 ? (magic angle). T1=1.09s; T2=521ms.

SE (iSQC)
Ave. Sig. Int.=8700

iDQC (??0??
Ave. Sig. Int.=240

iDQC (??45??
Ave. Sig. Int.=100

iDQC (??54.7??
Ave. Sig. Int.=29

GE 3T scanner. TE=60ms, TR=1s, t1 (dipolar evolution time) = 12ms, FOV=24cm, Slice thickness=10mm, Resolution 64 by 64.

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